Post Approval Submissions

Renewal Action Requested

ALERT: Modifications proposed as part of this renewal must be accomplished by editing the individual answers to the questions and data elements that make up the application. The modifications cannot be processed until the actual changes have been made throughout the application.

1. Renewal action requested by Principal Investigator (choose only one):

Study has always involved only analysis of data or specimens; there has never been any direct interaction or contact with subjects:

✘ A) Continue study as approved.

Study involves (or involved) direct interaction/intervention/contact with subjects:

✔ B) Continue study as approved, including enrollment of new subjects.

✘ C) Enrollment of new subjects closed; research-related intervention/interaction with previously enrolled subjects continues. ***Includes any interaction with subjects for the purpose of this study, including face-to-face visits during which procedures or tests will be completed.***

List the research activities that are ongoing.

--

✘ D) Enrollment of new subjects closed; subjects have completed all research-related intervention/interaction and the research remains active only for long-term follow-up of subjects. ***Includes telephone contacts, mail-in or web-based surveys, and continued review of medical records or registry (as described in the approved protocol).*** **In person contacts may include visits being conducted as part of routine clinical care where research-related activities include, questionnaires, surveys or interview (e.g., review of medical/health history).**

✘ E) All research-related interaction/intervention and long-term follow-up is now complete; renewal requested for data analysis only. ***If you have completed the study as described in protocol/application and are analyzing data for this study, your study is in data analysis. Once data analysis for this study has been completed and all data/specimens have been destroyed or stored of as described in your application, the study should be closed.***

Progress Report

1. Number of Subjects involved through direct contact or use of their data (for multi-site studies, include only subjects covered by this IRB) (Note: **b+d** should not be larger than **a**)

A. Total projected number as approved by IRB:	9999	9999 (Prior Response)
B. Total number of subjects included/enrolled to date (do NOT include 'screen failures')	1483	1462 (Prior Response)
C. Number of subjects included/enrolled since last renewal:	21	18 (Prior Response)
D. Number to be included/enrolled in upcoming year	150	150 (Prior Response)

E. Since initial approval, have any subjects been enrolled who are members of vulnerable/protected groups (children, pregnant women, nonviable neonates or neonates of uncertain viability, prisoners, cognitively impaired)?	No
Please enter the number of subjects enrolled for each group:	
Children	--
Pregnant women	--
Nonviable neonates or neonates of uncertain viability	--
Prisoners	--
Decisionally impaired individuals	--
F. Since initial approval, have you enrolled any individuals using an Informed Consent Short Form?	No
How many subjects?	--
Explain why you were not able to provide a full, translated consent form. --	

2. Have any subjects withdrawn voluntarily or been withdrawn from the study since the last renewal?

   No

3. Have there been any complaints about the research from subjects or others since the last renewal?

   No

4. Have there been any findings (e.g., publications, new information, study results) that alter the risk/benefit ratio or otherwise impact the study since the last renewal?

   No

5. Have there been any relevant multi-site reports that have not been previously submitted to the IRB?

   No

6. If this study has a Data and Safety Monitoring Committee (DSMC or DSMB), is there a report that has not been previously submitted to the IRB?

   No

7. Please review OHRE SOP 1401 on New Safety Information reporting

Select one of the following:	1. I have reported all deviations, identified within this review period, that qualify as New Safety Information per OHRE SOP 1401 (if any). All other deviations are documented in the Protocol Deviation Tracking Log (NOTE: Do NOT attach the Protocol Deviation Log to the application)

Please submit a New Safety Information (NSI) Submission(s) in IRBIS at this time and as applicable. In the NSI submission, include an explanation why the deviation(s) was not submitted promptly per OHRE SOP 1401 and a plan for ensuring timely submission going forward.

8. Has there been any new safety information related to the research that poses an increased risk to subjects or others that has not yet been reported to the IRB?

No

9. If the IRB approved modifications since the study was initially approved or last renewed, have all modifications approved by the IRB been implemented? Of particular importance are changes related to subject safety, such as re-consenting subjects to explain new study information/risks or the implementation of additional safety measures. (Note: If you have not had any modifications in this time period, select "Yes")

Yes

10. Has this study been reviewed by an external monitor or auditor since approved or last renewed?

No

11. Will you be obtaining consent (initial or re-consent) from subjects in the upcoming approval period?

Yes

Reminder: Please confirm consent forms are up to date.

12. Is any part of this study under the oversight of a local IRB or other ethics review committee?

No

Continuing with Renewals

1. Are you requesting any modifications to the study application, project personnel, the consent documents, or any related documents at the time of this renewal?

Yes

Changes to Project Personnel only?

No

Provide a brief non-technical summary of any changes you will be making to the study (i.e., study application, project personnel, and/or study documents.) The text you enter here will be reproduced in the IRB approval document, and should contain the details that you and/or your sponsor find relevant (e.g., master protocol/amendment version number and date). Typical summaries are 50-100 words. PLEASE NOTE: THIS SECTION MAY BE EDITED BY THE IRB FOR CLARITY OR LENGTH.

Please provide the description below:

Yes. The consent forms now can include the new name of the Center. Rather than having "National Health and Environmental Effects Research Laboratory" (old name of our laboratory), the consent form can include "Center for Public Health and Environmental Assessment" (new name of our center). Thanks.

Modification Specific Questions

9a. Is this study in Data Analysis only (i.e. enrollment, intervention and follow-up are complete)?	No
9b. Total number of subjects actively participating (i.e., Total number of subjects involved in the interventional part of this study. If the study is limited to data collection (e.g., surveys, questionnaires, collection of data from existing records), enter '0'):	9999
9c. Have the risks as described in A.6., consent form, or any other study document changed? *This may include new risks not previously listed, changes in frequency of known risks, or removal of previously listed risks.*	No

If yes, list any changes in potential risks
(E.g. Risks now include, pain in the abdomen, weight gain, low blood protein, dry eyes, liver injury, high blood sugar which may lead to diabetes. Dry mouth was listed as a common side effect (approximate incidence > 25%) and is now listed as a very common side effect (approximate incidence > 50%).
--

9d. Do you have plans to re-consent subjects as a result of this modification?	No
Are you planning to re-consent currently enrolled subjects as a result of this modification?	--
Are you planning to re-consent previously enrolled subjects as a result of this modification?	--

If yes, please describe your plans for re-consenting subjects; specify who will be responsible for re-consenting subjects and the time frame for doing so.
--

9e. Is this modification being submitted in response to New Safety Information?	No

If yes, explain, including whether this information is relevant to participants' willingness to continue.
--

General Information

1. General Information

1. Project Title

Effects of in Vitro Pollutant Exposure on Functional and Biochemical Characteristics of Human Pulmonary Cells in Normal Subjects

2. **Brief Summary**. Provide a **brief non-technical description** of the study, which will be used in IRB documentation as a description of the study. Typical summaries are 50-100 words. Please reply to each item below, retaining the subheading labels already in place, so that reviewers can readily identify the content. PLEASE NOTE: THIS SECTION MAY BE EDITED BY THE IRB FOR CLARITY OR LENGTH.

The purpose of this research is to study the response of cells and fluid to environmental agents during in-vitro assays (e.g. ecytokine release by epithelial cells and macrophages following exposure to air pollution particles.)

All subjects will be between the ages of 18 and 40 years in three groups: 1) healthy non-smoking young adults, 2) healthy young adults who are cigarette smokers, and 3) subjects with mild asthma by the NIH/NHLBI definition.

Subjects will have bronchoscopy (described in full in: Ghio AJ, Bassett M, Chall AN, Levin DG, Bromberg PA. Bronchoscopy in healthy volunteers. Journal of Bronchology 1998; 5:185-194).

2. Project Personnel

1. Will this project be led by a STUDENT (undergraduate, graduate) or TRAINEE (resident, fellow, postdoc), working in fulfillment of requirements for a University course, program or fellowship?

No

2. List all project personnel beginning with principal investigator, followed by faculty advisor, co-investigators, study coordinators, and anyone else who has contact with subjects or identifiable data from subjects.

- List ONLY those personnel for whom this IRB will be responsible; do NOT include collaborators who will remain under the oversight of another IRB **for this study**.
- If this is Community Based Participatory Research (CBPR) or you are otherwise working with community partners (who are not functioning as researchers), you may not be required to list them here as project personnel; consult with your IRB.
- If your extended research team includes multiple individuals with limited roles, you may not be required to list them here as project personnel; consult with your IRB.

The table below will access campus directory information; if you do not find your name, your directory listing may need to be updated.
If a change to the Principal Investigator is requested during the course of the study, a PI Change Form must be submitted.

University of North Carolina at Chapel Hill (UNC-CH)

Full Name	Credentials	Role	IRB Training	GCP	COI Number	Initial COI Disclosure	Potential Conflict	COI Review Process	COI Review Result
Andrew J. Ghio	--	Principal Investigator	✓	✗	19-54098	✓		Completed	No Conflict
Martha Almond	--	Co-investigator	✓	✓	19-54101	✓		Completed	No Conflict
Tracey Montilla	--	Co-investigator	✓	✓	19-54099	✓		Completed	No Conflict

Julie Wood	--	Co-investigator	✔	✖ 19-54100	✔	Completed	No Conflict

NOTE: The IRB database will link automatically to UNC Human Research Ethics Training database and the UNC Conflict of Interest (COI) database. Once the study is certified by the PI, all personnel listed (for whom we have email addresses) will receive separate instructions about COI disclosures. The IRB will communicate with the personnel listed above or the PI if further documentation is required.

3. If this research is based in a center, institute, or department (Administering Department) other than the one listed above for the PI, select here. Be aware that if you do not enter anything here, the PI's home department will be AUTOMATICALLY inserted when you save this page.

Department	Aux Services Affiliates: EPA

3. Funding Sources

1. Is this project funded (or proposed to be funded) by a contract or grant from an organization EXTERNAL to UNC-Chapel Hill?

Yes

Is UNC-CH the **direct** recipient of any Federal funding for this study? You should answer 'yes' *only* if you are the grantee. You should answer 'no' if you are the recipient of a sub-award or contractor under the grant.

No

Funding Source(s) and/or Sponsor(s)

Sponsor Name	UNC Ramses Number	Sponsor Type	Prime Sponsor Name	Prime Sponsor Type	Sponsor/Grant Number	Detail
EPA						view

2. Is this study funded by UNC-CH (e.g., department funds, internal pilot grants, trust accounts)?

No

3. Is this research classified (e.g. requires governmental security clearance)?

No

4. Is there a master protocol, grant application, or other proposal supporting this submission (check all that apply)?

- ✖ Grant Application
- ✖ Industry/Federal Sponsor Master Protocol
- ✖ Student Dissertation or Thesis Proposal
- ✖ Investigator Initiated Master Protocol
- ✖ Other Study Protocol

5. Is this a Clinical Study?
Check YES if this study involves research using human volunteers that is intended to add to medical knowledge. There are two main types of clinical studies: clinical trials and observational studies. Do NOT check yes merely because you are conducting research in a clinical setting or using clinical data.
Click here for additional definition of "Clinical Study"

No

4. Screening Questions

The following questions will help you determine if your project will require IRB review and approval.

The first question is whether this is RESEARCH (click for details)

1. Does your project involve a systematic investigation, including research development, testing and evaluation, which is designed to develop or contribute to generalizable knowledge? PLEASE NOTE: You should only answer yes if your activity meets all the above.

   Yes

The next questions will determine if there are HUMAN SUBJECTS (click for details)

2. Will you be obtaining information or biospecimens through intervention or interaction with the individual, and use, study, or analysis of the information or biospecimens? This would include any communication or interpersonal contact between investigator and subject such as using in-person or online questionnaires/surveys, interviews, focus groups, observations, treatment interventions, etc. PLEASE NOTE: Merely obtaining information FROM an individual does not mean you should answer 'Yes,' unless the information is also ABOUT them.

   Yes

3. Will you be obtaining, using, studying, analyzing, or generating identifiable private information or identifiable biospecimens collected through means other than direct interaction? This would include data, records or biological specimens that are currently existing or will be collected in the future for purposes other than this proposed research (e.g., medical records, ongoing collection of specimens for a tissue repository).
   OR
   Will you be using human specimens that are not individually identifiable for FDA-regulated in vitro diagnostic (IVD) device investigations?

   No

The following questions will help build the remainder of your application.

4. Will subjects be studied in the Clinical and Translational Research Center (CTRC, previously known as the GCRC) or is the CTRC involved in any other way with the study? (If yes, this application will be reviewed by the CTRC and additional data will be collected.)

   No

5. Does this study directly recruit participants through the UNC Health Care clinical settings for cancer patients **or** does this study have a focus on cancer or a focus on a risk factor for cancer (e.g. increased physical activity to reduce colon cancer incidence) **or** does this study receive funding from a cancer agency, foundation, or other cancer related group? (If yes, this application may require additional review by the Oncology Protocol Review Committee.)

   No

6. Is the UNC Chapel Hill IRB taking or being asked to take responsibility for the oversight of research by individuals, groups or organizations outside of UNC Chapel Hill? Or you are asking the UNC Chapel Hill IRB to cede review to an External IRB. If so, a reliance agreement will need to be executed prior to conducting any research activities. See guidance.

   No

Location

1. Are UNC-affiliated researchers involved in research conducted at any locations outside of the United States?

   No

Part A. Questions Common to All Studies

A.1. Background and Rationale

A.1.1. Provide a summary of the background and rationale for this study (i.e., why is the study needed?). If a complete background and literature review are in an accompanying grant application or other type of proposal, only provide a brief summary here. If there is no proposal, provide a more extensive background and literature review, including references.

Much investigation at the Human Studies Facility of the Environmental Protenction Agency focuses on determinination of a biological response by relevent exposures including ozone, other oxidant gases, air pollution particles, other particles, and endotoxin. Among the studies conducted are in vitro assays using pertinent cells (i.e. alveolar macrophages and respiratory epithelial cells). The collection of such cells from healthy volunteers is achieved during bronchoscopy. Alveolar macrophages are acquired by bronchoalveolar lavage and airway epithelial cells are obtained by bronchial brushes. In addition to the these cells, lavage fluid is also employed in studies focused on analysis of fluid phase constituents (e.g. albumin) and in vitro interactions with environmental exposures.

A.1.2. State the research question(s) (i.e., specific study aims and/or hypotheses).

The research question posed is how does the environmental exposure alter the in vitro response of the specific biological endpoint studied in the collected cells. Biological endpoints studied can include cell signaling (e.g. MAP Kinase activation), transcription factor activiation (e.g. nrf2 and nFkB activation), and mediator release (e.g. interleukin release).

A.2. Subjects

A.2.1. Total number of subjects proposed across all sites by all investigators (provide exact number; if unlimited, enter 9999):

9999

A.2.2. Total number of subjects to be studied by the UNC-CH investigator(s) (provide exact number; if unlimited, enter 9999):

9999

A.2.3. If the above numbers include multiple groups, cohorts, or ranges or are dependent on unknown factors, or need any explanation, describe here:

We are asking to study up to 150 subjects per year.

A.2.4. Do you plan to enroll subjects from these vulnerable or select populations:
If you will include children, prisoners or nonviable neonates or neonates of uncertain viability, please check the appropriate category below and complete the additional sections.

You should check "Pregnant women" if you specifically intend to recruit women who are pregnant or are not excluding pregnant women in biomedical research that is greater than minimal risk. Do not check if you are conducting a survey of the general public or conducting secondary data analysis or chart review not aimed at pregnant women.

Only check UNC-CH Student athletes, athletic teams, or coaches if you have specific plans to enroll these subjects. This is not applicable for intramural or club sports. For definitions and guidance see SOP 1201: Vulnerable subjects in research.

- ✖ Children (under the age of majority for their location)

Any minor subject who attains the age of majority during the course of the research study must provide consent as an adult, unless consent has been waived, which is requested in section D.3.1.

- ✖ Pregnant women
- ✖ Nonviable neonates or neonates of uncertain viability
- ✖ Prisoners, others involuntarily detained or incarcerated (this includes parolees held in treatment centers as a condition of their parole)

If an enrolled participant becomes incarcerated during the course of the research, they must be removed from the research project until such time as the IRB (and OHRP for NIH funded projects) approves the study to include prisoners, unless there is an immediate risk to the participant from ending treatments under the protocol.

- ✖ UNC-CH Student athletes, athletic teams, or coaches

A.2.5. Based on your recruitment plan and target sample population, are you likely to include any of the following as subjects? Select all that apply. This is not applicable to secondary data analysis or chart review.

Based on your responses, the consent form builder will insert the required text into your consent form template.

- ✖ Decisionally impaired individuals

(e.g., Mini mental state examination (MMSE), Montreal cognitive assessment (MOCA))

- ✖ Children who are wards of the State (Foster children)
- ✖ Non-English-speaking individuals
- ✖ UNC-CH Students
- ✖ UNC-CH Employees
- ✖ People, including children, who are likely to be involved in abusive relationships, either as perpetrator or victim.
This would include studies that might uncover or expose child, elder or domestic abuse/neglect. (See SOP Appendix A)

A.2.6. If any of the above populations are checked (excluding 'Decisionally impaired individuals' and 'Children who are wards of the State (Foster children)'), please describe your plans to provide additional protections for these subjects.

No Answer Provided

A.2.7. Age range of subjects:

Minimum age of subject enrolled	18
	years
Maximum age of subject enrolled	40
» If no maximum age limit, indicate 99	
	years

A.3. Inclusion/exclusion criteria

A.3.1. List required characteristics of potential subjects (i.e., inclusion and exclusion criteria). If not covered, list also characteristics that would preclude their involvement.

We plan to study about 150 volunteers each year. All subjects will be between the ages of 18 and 40 years in three main groups: 1) Healthy non-smoking young adults; 2) Healthy young adults who are cigarette smokers; and 3) Subjects with mild asthma by the NIH/NHLBI definition. Women who are pregnant will be excluded as fetal risk cannot be justified for these non-therapeutic procedures. Males and females of all ethnicities will be recruited.

A single subject may undergo bronchoscopy on more than one occasion. However, a minimum of 6 weeks must pass between procedures for an individual.

Inclusion criteria:

Healthy nonsmokers: 1) Healthy non-smoking young adult (18-40 years of age) volunteers. These individuals will have no respiratory symptoms on history, no abnormalities on exam, and normal pulmonary function testing. There has been less than 1 pack year total smoking with none in the 2 weeks prior to the procedure.

Asthmatics: Adults 18 to 40 years of age with a history of physician-diagnosed asthma which is mild in severity. These individuals will be healthy and experiencing mild persistent or mild intermittent asthma (NIH/NHLBI definition). There will be minimal symptoms on history, no abnormalities on exam, and normal to mild obstruction on pulmonary function testing..

Smokers: Healthy adult volunteers between 18 and 40 years of age who are active smokers with a total life-time history of cigarette use of at least 5 pack-years. These individuals will

have no respiratory symptoms on history, no abnormalities on exam, and normal pulmonary function testing.

A.3.2. Justify any exclusion based on race, gender or ethnicity

Exclusion criteria:

1. Including, but not limited to: any significant acute or chronic medical condition including cardiovascular disease, neurological disease, renal disease, liver disease, diabetes, other endocrinological disease, malignancy or autoimmune disease.
2. Pregnancy or nursing an infant.
3. Weight of 110 pounds or less
4. For asthmatics: any indication of moderate or severe asthma such as:

a. Physician directed emergency treatment for an asthma exacerbation within the preceding 12 months.

b. Any use of systemic steroid therapy during the last year or continuous use of inhaled steroids over a period of 1 month or longer during the past 6 months.

c. Regular use of cromolyn (except for prophylaxis of exercise induced bronchospasm) or any use of leukotriene inhibitors (Montelukast or Zafirlukast) within the past month.

d. Symptoms including: i) night-time symptoms of cough or wheeze greater than 1x/week;

ii) exacerbations of asthma more than 2x/week; iii) daily requirement for albuterol due to asthma symptoms (cough, wheeze, chest tightness).

4. Regular use of aspirin or other nonsteroidal anti-inflammatory drugs (which inhibit platelet function).

Temporary exclusions:

1. An asthma exacerbation requiring increased asthma medications for more than 1 day (and other than exercise induced asthma) within 1 month of bronchoscopy.

2. Viral upper respiratory tract infection or any acute infection requiring antibiotics within 6 weeks of bronchoscopy.

3. Medications (including over?the?counter preparations) during the two days prior to the bronchoscopy

4. Any food or fluids after midnight

A.3.3. Will pregnant women or women who become pregnant be excluded?

Yes

If yes, provide justification and describe the type and timing of pregnancy testing to be used:

A urine pregnancy test will be performed on all female subjects and a positive result will exclude the subject from further participation in this study.

A.4. Study design, methods and procedures

Your response to the next question will help determine what further questions you will be asked in the following sections.

A.4.1. Will you be using any **methods or procedures commonly used in biomedical or clinical research** (this would include but not be limited to drawing blood, performing lab tests or biological monitoring, conducting physical exams, administering drugs, or conducting a clinical trial)?

Yes

A.4.2. Describe the study design. List and describe study procedures, including a sequential description of what subjects will be asked to do, when relevant.

Subjects will undergo a physical examination including assessment for suitability for transnasal fiberoptic bronchoscopy at the Human Studies Facility by a board certified or board eligible pulmonologist. A blood sample will be obtained for a serum chemistry screen and a complete blood count with platelets and white blood cell differential. A urine pregnancy test will be performed on all female subjects and a positive result will exclude the subject from further participation in this study. Subjects will have spirometry as part of the physical examination.

A single blood sample totaling no more than 100 ml (7 oz) will be obtained from you and a small tube (IV) will be placed in a vein for potential use in administering fluids. Bronchoscopy (described in full in: Ghio AJ, Bassett M, Chall AN, Levin DG, Bromberg PA. Bronchoscopy in healthy volunteers. Journal of Bronchology 1998; 5:185-194). The subjects may be pre-medicated with atropine (0.5 mg IV) and nasal oxygen will be administered during the procedure. We have found that premedication with sedatives (midazolam) or with opiates (demerol) is not required for young, healthy subjects. Avoidance of these drugs reduces procedure risk and markedly shortens post-procedure recovery time. Topical lidocaine anesthesia will be used for subject comfort and to prevent cough, with a maximum of 15 ml of 2% lidocaine solution (300 mg lidocaine) given. Electrocardiographic and pulse oximeter monitoring will be maintained throughout. After the airways are visualized, the bronchoscope tip is wedged in a 4th-6th order bronchus (lingular and right middle lobe) for bronchial lavage. A total volume of 270 cc of sterile saline, one aliquot of 20 cc and 5 additional aliquots of 50 cc each, will be injected and immediately aspirated through the channel in the bronchoscope using a syringe. The lavage fluid aliquots will be put in polypropylene tubes and kept on ice until processed. After topical application of 1% lidocaine, a total of up to 6 brush biopsies will then be obtained from either a) the lower trachea, main, and lobar bronchi or 2) the small airways.

For large airways (the lower trachea, main, and lobar bronchi), a cytology brush

(Bronchoscope Cytology Brush; Bard, Tewksbury, MA) is applied to the region under direct visualization. For a single brushing, six passes, each with a linear excursion of 2-5 cm, are made with the brush along the endobronchial surface. Bleeding should be slight but, if persistent, will be controlled with 2.0 ml 1:10,000 epinephrine. Rather than brushings of a large airway, a volunteer may have brushings of a small airway. To accomplish this, a brush is deployed several centimeters more distally along the airway than the large airway brush. Following positioning at the orifice of a right and/or left lower lobe subsegmental bronchus, the sheath is advanced carefully 3-5 cm. The brush is gently moved in a proximal/distal repetition for 6 excursions. The brush is withdrawn into the sheath and then the sheath is removed from the scope. The complications of a brush in a small airway is comparable to that of such a procedure in the large airway. This includes minor bleeding.

Subjects are observed and monitored for a minimum of one and 2 hours after the procedure in the on-site medical station by a technician with physician supervision. At discharge subjects will be symptom-free. At least 2 physicians, including the responsible bronchoscopist, will be available (24 hours daily) to subjects who develop any symptoms after discharge. The subject is discharged by a physician and is provided with the names and telephone number of the bronchoscopist. The subject is contacted 24 hours post-bronchoscopy to ask about any untoward effects.

A.4.3. If subjects are assigned or randomized to study "arms" or groups, describe how they are assigned.

- *Describe the methods of computing the randomization schedule (if any) and maintaining blinding (if any).*
- *Who will perform these computations?*
- *How will you verify each subject's eligibility prior to randomization?*

No Answer Provided

A.4.4. Describe any follow up procedures.

None

A.4.5. Once this study has been approved by the IRB, for how many months or years will this study be active (you are collecting data or have access to identifiers)?

The history and physical examination and blood work (CBC and chemistries) necessitates approximately 3 hours. On the day of the bronchoscopy, the subject will be at the Human Studies Facility for about 3-4 hours. The bronchoscopy procedure itself requires only about 30 minutes. On any given bronchoscopy day, a second eligible subject will be recruited to be on standby. This ensures that we will be able to obtain samples on a given day. If a standby subject is not needed, he or she will discharged within approximately 45 minutes of arrival.

Bronchoscopy specimens will be collected under this protocol for a total of 40 years.

A.4.6. Will this study use any of the following methods?

- ✗ Audio Recording
- ✗ Video Recording
- ✗ Behavioral observation - (e.g., Participant, naturalistic, experimental, and other observational methods typically used in social science research)
- ✓ Pencil and paper questionnaires or surveys
- ✗ Electronic questionnaires or surveys
- ✓ Telephone questionnaires or surveys
- ✗ Interview questionnaires or surveys
- ✗ Other questionnaires or surveys
- ✗ Focus groups
- ✗ Diaries or journals
- ✗ Photovoice
- ✗ Still photography

A.4.7. If there are procedures or methods that require specialized training, describe who (role/qualifications) will be involved and how they will be trained.

Bronchoscopist is board-eligible or -certified pulmonologist

A.4.8. Are there cultural issues, concerns or implications for the methods to be used with this study population?

No

A.4.A. Biomedical methods and procedures

A.4.A.1. Is this an interventional study?

No

Distinguish what is being done specifically for this research from procedures that would be done anyway for clinical care:

No Answer Provided

A.4.A.2. If the study involves the use of placebo control, provide justification

None

A.4.A.3. Will this study involve drugs, biologics or other substances (such as a botanical or dietary supplement)?
For guidance on dietary supplements, see Section VI, C FDA guidance document UCM229175.pdf

Yes

Please list all drugs/biologics or other substances to be administered. Provide separate entries for combination drugs and describe in procedures. For complicated dosing schedules (e.g., dose escalation studies), provide range below and detailed information in procedures.

Generic Name	Brand Name	Dose (a)	Frequency (a)	Route(s)	Status of Drug	Detail
Lidocaine suspension, jelly, and solution		Less than 300 mg lidocaine solution is instilled through the bronchoscope		Gargled, sniffed, and instilled through the bronchoscope	FDA-approved use	view
Atropine sulfate		0.6 mg	Pre-medication, provided once	Intravenous	FDA-approved use	view
Epinephrine		1:10,000; 1.0 mL per instillation	A total of 2.0 mL can be used	Through the bronchoscope	FDA-approved use	view

A.4.A.4. Is there an Investigational New Drug application (IND) for this study?

No

Please check below:

- ✘ This study does not involve drugs, biologics or other substances.
- ✘ I am using a U.S. commercially available agent, consistent with labeling.
- ✘ I am studying a botanical substance or dietary supplement intended to affect the structure and/or function of the body; it is **not** intended to cure, treat, mitigate, prevent or diagnose disease, including its associated symptoms.

A.4.A.5. When the intent of a clinical investigation is to collect information about the safety or effectiveness of a device, the need for an Investigational Device Exemption (IDE) must be evaluated. Please review the Investigational Device Guidance document prior to completing this section. Your response to the following questions will determine if an IDE is needed.

A. Select the response that best describes your investigation:

5. None of the above.

A.4.A.6. Does your study involve any of the following? (check all that apply)

- ✘ Embryonic stem cells
- ✘ Fetal tissue
- ✘ Genetic testing (see GINA and GWAS)
- ✘ Clinical laboratory tests

If McLendon Labs will do the testing, you must complete the appropriate form found at UNC Health Care and submit to them for review.

- ✘ Testing for communicable diseases that have mandated reporting requirements (link to state guidance)
- ✔ Point of Care Testing (POCT), which is CLIA-approved testing done at the "bedside" or site of care by hospital or clinic personnel (not by subject). Examples include urine pregnancy testing, glucose monitoring, etc.

If McLendon Labs will do the testing, you must complete the POCT form found at UNC Health Care and submit to them for review.

✖ If your study utilizes **radiopharmaceuticals** to address basic science questions, an IND is not necessary.
Instead, your study will be reviewed/approved by the Radioactive Drug Research Committee (RDRC); approval by the Radiation Safety Subcommittee (RSS) is not required.
If you have questions about the RDRC approval process, please contact Dede Corvinus.

✖ Diagnostic or therapeutic ionizing radiation, or radioactive isotopes (not covered under 21 CFR 361.1), which subjects would not receive otherwise if not participating in this research study. Do not check if all radiation is administered as standard of care.
Do check if your study includes views/scans that represent no greater than minimal risk as determined by the Radiation Safety Sub-committee.
Application for Human Use of Radiation in Research.

✖ Gadolinium administered as a contrast agent

✖ IBC (Institutional Biosafety Committee) - Recombinant DNA or gene transfer to human subjects

✖ Any research activities conducted in the UNCHC Perioperative areas. This includes Pre-care, Pre-op, Operating room and PACU.
You must complete the Checklist for Perioperative Services and return it to moe_lim@med.unc.edu

✖ Any form of medical imaging (ultrasound, MRI, CT, X-ray, PET-CT, PET-MRI)

A.4.A.7. Will your study involve storage of specimens for future unspecified research?

Yes

Please explain:

Aliquots of aceullar lavage fluid (5 and 1 mL) will be stored in -80 degree freezers in the basement of the Human Studies Facility. The only identifier on the tube is the procedure number.

Will any personal identifiers or codes be retained with the specimens that would allow anyone to link the specimen back to an individual subject?

No

A.5. Benefits to subjects and/or society

A.5.1. Describe how this study will contribute to generalizable knowledge that will benefit society.

Society will benefit because these studies should provide new information relevant to human disease after exposure to air pollution. Design of new therapeutic strategies, and identification of new targets for therapeutic development, may result from these investigations.

A.5.2. Does this study have the potential for direct benefit to individual subjects in this study?

Yes

Consider the nature, magnitude, and likelihood of any direct benefit to subjects. If there is no direct benefit to the individual subject, say so here and in the consent form, if there is a consent form. Do not cite monetary payment or other compensation as a benefit.

Explain

Subjects selected will receive the benefit of a medical examination that includes blood work and spirometry at no charge. Subjects will have access to their records with a written release form. The medical staff will explain to each subject any findings of note regarding his/her overall health status. All subjects will have the opportunity to speak with a pulmonologist to discuss his or her own symptoms and concerns.

A.5.3. Are there plans to communicate the results of the research OR results of any clinical tests administered for the research back to the subjects?

No

A.6. Risks and measures to minimize risks

For each of the following categories of risk you will be asked to describe any items checked and what will be done to minimize the risks.

A.6.1. Psychological

- ✗ Emotional distress
- ✗ Embarrassment
- ✓ Consequences of breach of confidentiality (Check and describe only once on this page)
- ✗ Other

A.6.2. Describe any potential psychological risks checked above and what will be done to minimize these risks

All records are kept in a locked room in the Human Studies Facility. Access to the room is limited to the personnel in the Medical Station who know the combination required for entrance.

A.6.3. Social

- ✗ Loss of reputation or standing within the community
- ✗ Harms to a larger group or community beyond the subjects of the study (e.g., stigmatization)
- ✗ Consequences of breach of confidentiality (Check and describe only once on this page)
- ✗ Other

A.6.4. Describe any potential social risks checked above and what will be done to minimize these risks

All records are kept in a locked room in the Human Studies Facility. Access to the room is limited to the personnel in the Medical Station who know the combination required for entrance.

A.6.5. Economic

- ✗ Loss of income
- ✗ Loss of employment or insurability
- ✗ Loss of professional standing or reputation
- ✗ Loss of standing within the community
- ✗ Consequences of breach of confidentiality (Check and describe only once on this page)
- ✗ Other

A.6.6. Describe any potential economic risks checked above and what will be done to minimize these risks.

All records are kept in a locked room in the Human Studies Facility. Access to the room is limited to the personnel in the Medical Station who know the combination required for entrance.

A.6.7. Legal

- ✗ Disclosure of illegal activity
- ✗ Disclosure of negligence
- ✗ Consequences of breach of confidentiality (Check and describe only once on this page)
- ✗ Other

A.6.8. Describe any potential legal risks checked above and what will be done to minimize these risks

All records are kept in a locked room in the Human Studies Facility. Access to the room is limited to the personnel in the Medical Station who know the combination required for entrance.

A.6.9. Physical

- ✓ Medication side effects
- ✗ Pain
- ✓ Discomfort
- ✓ Injury
- ✗ To a nursing child or a fetus (either through mother or father)

A.6.10. Describe any potential physical risks checked above, including the category of likelihood and severity, and what will be done to minimize these risks. Where possible, describe the likelihood of the risks occurring, using the following terms:

- Very Common (approximate incidence > 50%)
- Common (approximate incidence > 25 - 50%)
- Likely (approximate incidence of > 10 - 25%)
- Infrequent (approximate incidence of > 1 - 10%)
- Rare (approximate incidence < 1%)

Describe severity of risks using the following grading scale:

- Mild- No disruption to the subject's ability to perform daily activities; may include non-prescription intervention only
- Moderate- Temporary interference with daily activities; may include prescription intervention
- Severe- Interference with daily activities; medically significant but not life threatening
- Life threatening

Examples:

Rare (< 1%) and Severe: blindness
Rare (< 1%) and Mild: dry skin, dry mouth, transient headache

If you are using these terms differently than described above, please provide your study-specific definitions.

Phase 1 trials: Due to limited experience, incidence may be better described as the number of events that have occurred in the total number of animals/humans studied.

There are several risks associated with performing bronchoscopy, although these risks are exceedingly small when bronchoscopy is performed on young healthy subjects, the type of people involved in this study.

The primary risk of bronchoscopy is discomfort in the nose and throat, which is caused by having the bronchoscope inserted through the nose and passed through the back of your throat to reach the trachea (windpipe) and the airways leading to the lungs. This discomfort is alleviated with topical lidocaine, which you will gargle and inhale prior to beginning the procedure. If you are suffering from discomfort in your nose and throat because they are not adequately anesthetized, you can request that more lidocaine be used, however, there is a limit to the maximum amount of lidocaine that can be given. If you are unable to tolerate the passage of the bronchoscope thorough your nose and throat because of pain in spite of having received the maximum allowable amount of lidocaine, the procedure will be immediately terminated.

A second risk of having bronchoscopy performed is coughing. Coughing is caused by irritation from the bronchoscope itself or the instruments used to obtain the biopsy material. Lidocaine liquid can be sprayed into your airways thorough the bronchoscope to relieve coughing. If the coughing is uncontrollable even with the use of the maximum amount of

lidocaine, the procedure will be stopped immediately.

Lower airway bleeding can also occur from injury to the airway wall caused by the bronchoscope or the brush biopsies (both large and small airway brushes). This bleeding is usually very minor (only a few milliliters of blood are lost). The bleeding resolves spontaneously within several minutes. If the bleeding is mild to moderate, epinephrine (adrenalin) can be sprayed on the bleeding site through the bronchoscope to hasten the clotting.

The lidocaine used for anesthesia during the procedure can have some adverse effects because some of the lidocaine can be absorbed into the blood stream from the nose and lungs. If you are allergic to lidocaine, you could develop itching, hives, difficulty breathing, and possibly shock (a dangerous drop in blood pressure). This risk is minimal, but you will be excluded from participating in this study if you are allergic to lidocaine or any other topical anesthetic that is commonly used in minor surgical or dental procedures. Lidocaine can also cause symptoms in your central nervous system (confusion, tremor, euphoria, or, rarely, seizures) or heart rate disturbances (very fast or very slow heart rate) if an excessive dose of medication is used. Finally, a death in a volunteer receiving an overdose (over 1000 milligrams) of lidocaine during bronchoscopy has been reported from Rochester, New York. However, no serious side effects of this medication have been noted at lower doses such as those described in this protocol which uses up to 360 milligrams of lidocaine during the entire procedure. If any problems develop secondary to the use of lidocaine, Dr. Ghio and the physician on duty that day at the Human Studies Division of the EPA will be available to handle these problems.

Atropine, the medication possibly given to you by vein before the procedure starts, is given to help prevent your pulse from falling when the bronchoscope is first put into your airway. Atropine can cause you to have a dry mouth and nose as well as an increased pulse for about 30 to 60 minutes after it is given. These side effects are not harmful to you, and they wear off within 30 to 60 minutes after the drug is given.

The placement of an IV catheter in your arm can cause some pain. However, the IV is placed by a registered nurse who is very experienced in this technique, and the pain is very minor, usually resolving very soon after the IV catheter is in place. Rarely, placement of an IV catheter can result in the formation of a hematoma (bruise) at the site of the IV after it is removed. Also, a rare complication of IV placement is skin infection or an infection of the vein in which the IV catheter has been placed. The risk of getting an infection from the IV are minimized by the nurse's use of sterile technique of place the catheter. If you do have signs of infection at the IV site (redness, warmth, painful skin, swelling) after completion of the procedure, you will need to contact the EPA medical station (966?6232) or the physician who performed the bronchoscopy. You are not at increased risk by having blood drawn through the IV catheter.

Some subjects who undergo bronchoscopy may have a low grade fever (less than 101 degrees Fahrenheit) after the procedure is completed. This fever is almost always benign and usually resolves within 24 hours. Nevertheless, a persistent fever or any temperature of greater than 101 degrees Fahrenheit might mean that you have a infection, particularly pneumonia.

Therefore, if you have any fever greater than 101 degrees Fahrenheit after the bronchoscopy or a fever that doesn't resolve in 24 hours after the procedure is completed, you should contact the EPA medical station or the physician who performed the bronchoscopy so that arrangements can be made for you to be examined by one of the physicians at EPA. To prevent fever, you are provided ibuprofen (or acetaminephrine if preferred) as you leave. You will be called 24 hours after the procedure to check on your condition. In addition, there may be uncommon or previously unrecognized risks that might occur.

A.6.11. Unless already addressed above, describe procedures for referring subjects who are found, during the course of this study, to be in need of medical follow-up or psychological counseling

The subject is contacted 24 hours post-bronchoscopy to ask about any untoward effects.

A.6.12. Are there plans to withdraw or follow subjects (or partners of subjects) who become pregnant while enrolled in this study?

No

A.7. Data and safety monitoring

A.7.1. When appropriate, describe the plan for monitoring the data to ensure the safety of participants. These plans could range from the investigator monitoring subject data for any safety concerns to a sponsor-based data and safety monitoring board or committee (DSMB, DSMC, DMC), depending on the study. For studies that do not raise obvious safety concerns, you may still describe your plans for monitoring the study as it progresses.

Electrocardiographic and pulse oximeter monitoring will be maintained throughout the study. Subjects are observed and monitored for a minimum of one and 2 hours after the procedure in the on-site medical station by a technician with physician supervision. At discharge subjects will be symptom-free. At least 2 physicians, including the responsible bronchoscopist, will be available (24 hours daily) to subjects who develop any symptoms after discharge. The subject is discharged by a physician and is provided with the names and telephone numbers of the bronchoscopist and one other physician.

A.7.2. If not already addressed above, describe the plans for aggregate review of unanticipated problems (including but not limited to adverse events) across all sites, in order to monitor subject safety.

The investigators review all deviations and reports of untoward events weekly.

A.7.3. What are the criteria that will be used to withdraw an INDIVIDUAL SUBJECT from this study or halt the research intervention (e.g., abnormal lab tests, allergic reactions, failure or inability to comply with study procedures, etc.)?

An allergic reaction to lidocaine or inability to comply with the bronchoscopy would necessitate withdrawal of the subject from the study.

A.7.4. Are there criteria that will be used to stop the ENTIRE STUDY prematurely (e.g., safety, efficacy, unexpected adverse events, inability to recruit sufficient number of subjects, etc.)?

No

A.7.5. Will this study involve a data and safety monitoring board or committee?

No

A.8. Data analysis

A.8.1. Describe the analytical methods to be used (qualitative or quantitative)

Not applicable

A.8.2. Explain how the sample size is sufficient to achieve the study aims. This might include a formal power calculation or an explanation of why a small sample is sufficient (e.g., qualitative research, pilot studies)

Not applicable

A.9. Identifiers

A.9.1. Check which of the following identifiers you already have or will be receiving, or select "None of the above."

- ✔ Names (this would include names/signatures on consent forms)
- ✔ Telephone numbers
- ✔ Any elements of dates (other than year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death. For ages over 89: all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 and older
- ✔ Any geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code and their equivalent geocodes (e.g. GPS coordinates), except for the initial three digits of a zip code
- ✘ Fax numbers
- ✔ Electronic mail addresses
- ✔ Social Security numbers
- ✘ Medical record numbers
- ✘ Health plan beneficiary numbers
- ✘ Account numbers
- ✘ Certificate/license numbers
- ✘ Vehicle identifiers and serial numbers (VIN), including license plate numbers
- ✘ Device identifiers and serial numbers (e.g., implanted medical device)
- ✘ Web universal resource locators (URLs)
- ✘ Internet protocol (IP) address numbers
- ✘ Biometric identifiers, including finger and voice prints
- ✘ Full face photographic images and any comparable images
- ✘ Any other unique identifying number, code, or characteristic, other than dummy identifiers that are not derived from actual identifiers and for which the re-identification key is maintained by the health care provider and not disclosed to the researcher

✖ None of the above

A.9.2. For any identifiers checked, how will these identifiers be stored in relationship to the research data?

✔ with the research data (i.e., in the same data set and/or physical location)

✖ separate from the research data (i.e., coded with a linkage file stored in a different physical location)

Provide details about the option you selected above:

--

A.9.3. Are you collecting Social Security Numbers to be used as a unique identifier for study tracking purposes for national registry or database? (Do not check yes if collecting SSN *only* for payment purposes; this will be addressed later.)

Yes

Please justify

Names, addresses, and U.S. tax payer identification numbers (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. If payment equals or exceeds $600 per calendar year for U.S. persons, the amount will be reported to the Internal Revenue Service on Form 1099. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

A.10. Confidentiality of the data

A.10.1. Describe procedures for maintaining confidentiality of the data you will collect or will receive (e.g., coding, anonymous responses, use of pseudonyms, etc.).

All data is kept in a locked records room in the Human Studies Facility. Access to the room is limited to the personnel in the Medical Station who know the combination required for entrance.

A.10.2. Describe how data will be transmitted among research team (i.e., personnel listed on this application).

Data is not transmitted among research team members

A.10.3. Are you collecting sensitive information such as sexual behavior, HIV status, recreational drug use, illegal behaviors, child/physical abuse, immigration status, etc?

No

A.10.4. Do you plan to obtain a federal Certificate of Confidentiality for this study? Please note that all ongoing or new research funded by NIH as of December 13, 2016 that is collecting or using identifiable information is automatically issued a Certificate of Confidentiality (CoC). You should also select “Yes” if your study is NIH funded and has been issued a CoC under this updated NIH policy.

No

A.10.5. If this study is limited to data collection by survey or interview, discuss the potential for deductive disclosure (i.e., directly identifying subjects from a combination of indirect IDs).

Not relevant to this study

A.10.6. Will any of the groupings or subgroupings used in analysis be small enough to allow individuals to be identified?

No

A.11. Data sharing and transmission

A.11.1. Check all of the following who will receive **identifiable data** (contains any of the 18 identifiers listed above) outside the immediate research team (i.e., not listed as personnel on this application)? *

- ✔ No one
- ✘ Coordinating Center
- ✘ Statisticians
- ✘ Consultants
- ✘ Other researchers
- ✘ Registries
- ✘ Sponsor and/or its designee(s)
- ✘ External labs for additional testing
- ✘ Journals
- ✘ Publicly available dataset
- ✘ Other

A.11.2. For any recipients checked above, explain the confidentiality measures to be taken

No Answer Provided

A.12. Post-study disposition of identifiable data or human biological materials

A.12.1. Describe your plans for disposition of data or human biological specimens that are identifiable in any way (directly or via indirect codes) once the study has ended. If you plan to destroy linkage codes or identifiers, describe how and when this will be done.

There is no data or specimens which are identifiable.

Part B. Direct Interaction

B.1. Methods of recruiting

B.1.1. Check all the following means/methods of subject recruitment to be used:*

- ✘ In person
- ✘ MyChart

Use of MyChart for research recruitment purposes is currently available only to studies which meet specific criteria to participate in a pilot test. Please contact Stephanie Deen if you would like to see if your study meets the criteria for this use.

- ✔ Participant pools
- ✖ Presentation to classes or other groups
- ✖ Letters
- ✖ Flyers
- ✖ Radio, TV recruitment ads
- ✔ Newspaper recruitment ads
- ✔ Website recruitment ads
- ✔ Telephone script
- ✔ Email or listserv announcements
- ✔ Follow up to initial contact (e.g., email, script, letter)
- ✖ Other

B.1.2. Research for Me @ UNC is the public-facing, comprehensive, online portfolio of human subjects research at UNC and of applicable studies at UNC affiliates. Study teams may choose whether to submit basic or recruitment information for inclusion on the site.

- Select one of the three listing options below.
- For either the Core or Recruitment Information Listing, complete the REDCap form via the weblink (5-10 minutes, once per study).
- A PDF of the listing will be emailed to the PI and contacts listed on the form. It can also be found on Researcher Dashboard.

For Recruitment Information Listing, this PDF should be uploaded as an Attachment to your IRB application.

Core Information Listing

Basic study registration information will be displayed until enrollment closes; team contact information will not be visible to the public. Retain PDF for your records. view example

To request optimization of your listing language or if you have any questions about Research for Me @UNC, please email research_for_me@unc.edu.
To update an existing study listing: Edit or manage this listing via Researcher Dashboard. FAQs and additional guidance are also available.

B.1.3. Describe how subjects will be identified

Subject recruitment, telephone screening and administration of questionnaires will be carried out by a firm contracted by the US EPA, following the procedures outlined in this proposal. Every effort will be made to recruit women and members of racial minority groups into this study. Advertisements will be placed in various publications including student newspapers at the University of North Carolina at Chapel Hill (The Daily Tarheel) and Duke University (The Chronicle). Volunteers will be asked to call the recruitment office. During the telephone interview, the volunteers will receive information regarding teh study and their eligibility status will be assessed. Volunteers whose responses indicate that they are likely to meet the study criteria will be asked to come into recruitment.

Potential volunteers will self identify in response to the advertising described above. The exception will be for those identified from a pool of previous volunteers who are selected based on study eligibility criteria, who are then offered the study via an IRB approved email or phone script. After they are provided information about the study, they will elect whether or not to respond.

B.1.4. Select any of the following procedures solely conducted for screening, recruiting, or determining the eligibility of prospective human subjects. (Note: you should only collect the minimal information needed for these purposes.)

- ✖ Obtain information through oral or written communication with the prospective subject or legally authorized representative
  This includes online, telephone, or in-person screening questionnaires or interviews.
- ✖ Obtain already collected identifiable private information or records
  Examples include review of medical charts, data repositories, and administrative records.
- ✖ Reviewing/testing identifiable biospecimens by accessing stored biospecimens and related information
- ✖ None of the above

B.1.5. For any selections made, please describe the procedures. (Respond “N/A” if “None of the above” is selected.)

N/A

B.1.6. For any information collected for these purposes, please describe when and how you will destroy the data if the participant declines to participate or is not eligible. (Respond “N/A” if “None of the above” is selected.)

N/A

B.1.7. Describe how and where subjects will be recruited and address the likelihood that you will have access to the projected number of subjects identified in A.2.

Subjects generally will be recruited from the local Research Triangle area. Recruitment of healthy adults ages 18 to 40 without asthma who qualify for bronchoscopy has not been problematic. During a 3-year period from Oct 1, 2009 through Sep 30, 2012, Westat spoke with 604 callers ages 18 to 40, 111 whom were calling specifically for bronchoscopy and another 68 for any studies available. One-hundred twenty-one volunteers, about 40 people per year, qualified for bronchoscopy. Recruitment of adults with mild asthma for this study has been more difficult. During the same time period Westat spoke with 175 people with asthma, 31 calling specifically for bronchoscopy and 7 for any studies available. Only 13 people, about 4 per year, qualified for the mild asthma arm of the study. Recruitment materials for these groups are attached.

B.1.8. Describe how you will protect the privacy of potential subjects during recruitment

Emails will be sent from password protected computers with email stored on secure servers. Email subject lines will state either “Study at the US EPA” or “Your appointment at the EPA Human Studies Facility”. All phone calls and phone screening interviews will be conducted from private offices in the EPA Human Studies Facility. On site screening will also be conducted in private offices so that no personal information is shared with other research volunteers. More than one volunteer may be present in the waiting room at one time, but personal information will not be discussed in that area.

B.1.9. Describe how subjects will be contacted, if not addressed above

Potential subjects will contact WESTAT by phone, or by email from the recruitment web site (www.epastudies.org). WESTAT will respond either by phone or by email.

B.1.10. Describe who (by role) will do the recruiting

WESTAT, Inc. will provide recruitment services to support this study. WESTAT is a Contract Research Organization under contract with the US EPA since 1998 to provide support services for human research at the Human Studies Facility in Chapel Hill, NC. WESTAT staff members are CITI and COI trained and certified.

B.1.11. Describe efforts to ensure equal access to participation among women and minorities

See above

B.2. Protected Health Information (PHI)

Protected Health Information (PHI) is any identifiable information about the subject's health that relates to their participation in this research and is obtained from sources other than the subject, such as medical records, health care providers, insurance plans, etc. *more*

B.2.1. Are you requesting a limited waiver of HIPAA authorization?
If you need to access Protected Health Information (PHI) to identify potential subjects who will then be contacted, you will need a limited waiver of HIPAA authorization (see SOP 1801, 2.3). This does not apply to situations where you will never contact subjects directly (e.g., retrospective chart review), in which case you should request a full waiver under section D.

No

B.2.2. Will you need ongoing access to PHI (e.g., medical records) to conduct the study, beyond the identification of potential subjects as addressed above? In this case you will need to obtain a signed HIPAA Authorization from each subject.

No

B.3. Subject Contact, Duration and Privacy

B.3.1. Number of contacts per subject (contacts includes in-person, telephone, email, mailings, etc.)

After medical clearance for participation, there will be phone contact for an opinion on whether he/she wishes to have bronchoscopy. This is followed by the actual procedure (1).

B.3.2. Duration of each contact. If multiple contacts, provide the range or average time for each contact.

On the day of the bronchoscopy, the subject will be at the Human Studies Facility for about 3-4 hours. The bronchoscopy procedure itself requires only about 30 minutes. On any given bronchoscopy day, a second eligible subject will be recruited to be on Astandby@. This ensures that we will be able to obtain samples on a given day. If a standby subject is not needed, he or she will discharged within approximately 45 minutes of arrival.

B.3.3. Total duration of individual subject's participation, including follow up evaluation, if applicable

See above

B.3.4. Where are you studying subjects or obtaining their data?

✔ Non-healthcare setting
✖ Healthcare setting

B.3.5. Provide more information about the location(s) where research will be conducted (e.g., if UNC Medical Center is checked in #4 above and study visits will be conducted in the CTRC, enter “CTRC” here.)

Human Studies Facility

B.3.6. Describe procedures that will ensure privacy of the subjects in this study. Examples include the setting for interviews, phone conversations, or physical examinations; communication methods or mailed materials (e.g., mailings should not indicate disease status or focus of study on the envelope)

Interviews (phone and questionnaire) are conducted by Westat in private offices. Physical examinations are conducted in examination rooms.

B.4. Incentives for participation

B.4.1. Are there incentives (monetary or non-monetary) for subjects to participate or are you reimbursing subjects for study-related costs (e.g., travel, parking, hotel accommodations or childcare)?

Yes

A. Please describe any incentives and/or reimbursements for study-related costs separately below.

Subjects will receive a total sum approximating $425 for completion of the entire protocol:

Bronchoscopy including 1 venipuncture	$400.00
Brush biopsies (usually takes six brushings)	$25.00

Names, addresses, and U.S. tax payer identification numbers (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. If payment equals or exceeds $600 per calendar year for U.S. persons, the amount will be reported to the Internal Revenue Service on Form 1099. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

Any eligible subject who is unable to complete the bronchoscopy procedure for voluntary or involuntary reasons will receive full compensation for his/her participation to that point; however a subject who arrives in the lab for the procedure having not followed instructions (having food, taking NSAIDs or aspirin, or failing to report cold or flu symptoms the day prior to the bronchoscopy) will be compensated $15 for his/her time, but will not receive compensation for the bronchoscopy.

All subjects who volunteer to be on standby will be compensated $40 for their time. If this subject actually undergoes bronchoscopy, he/she will be compensated the full amount as noted above. In addition, all subjects will be reimbursed for parking costs and travel expenses will be paid for subjects who live outside of Chapel Hill. All subjects will be given snacks and juice after the required NPO time has elapsed.

B. Specify the schedule for incentives and if/how this will be prorated if the subject withdraws (or is withdrawn) from the study prior to completing it.

See above

C. For compensation in foreign currency, provide a US dollar equivalent.

We do not pay in foreign currency

D. Discuss the potential for coercion, given factors like the amount of the incentive, the age of the subjects, the purchasing power in foreign countries, the time involved and complexity of procedures, etc.

Over the many years of doing bronchoscopy in this same age group, a coercion factor has never been described by any volunteer.

E. If the subjects are children who will receive the compensation, i.e., the child, the parents or both?

No children are included in this study.

B.4.2. Are you collecting Social Security numbers or ITIN for payment and/or tax-related purposes?

Yes

Check all that apply

- ✔ Processing payments greater than $200 per year, to support IRS reporting
- ✖ Processing payments of any amount through UNC-CH Accounts Payable

B.5. Costs to be borne by subjects

B.5.1. Will there be any costs that subjects will incur related to participation in the study? Do not include costs for standard care for which patients would be billed if they were not in this study. Also do not include the time spent participating in the study.

No

Part C. Existing Data, Records, Specimens

C.1. Data Sources

C.1.1. What existing records, data or human biological specimens will you be using? (Indicate all that apply or select 'None of the above'):

- ✖ Medical records in any format.

  ALERT: You must check both boxes: 1) Medical records in any format and 2) Electronic medical record using Epic, or you/your study team will not be granted access to Epic for research purposes.

- ✖ Electronic medical records using Epic, WebCIS or other electronic system
- ✖ Carolina Data Warehouse for Health (CDW-H) (for UNC and its affiliates only)
- ✖ Carolinas Collaborative Data Request and Review Committee (DRRC)
- ✖ Paper medical records

If you access the medical records of fewer than 50 patients under a full or limited waiver of HIPAA, submit a copy of your IRB approval letter and a completed Research Disclosure Form to Health Information Management (HIM). Do not submit this information to the IRB. For additional information about this process, you should contact HIM directly at : 919-595-5591 or 919-966-1225 or 919-595-5580.

- ✖ Data already collected from another research study

Were the investigators for the current application involved in the original collection?	--
✖ Patient specimens (tissues, blood, serum, surgical discards, etc.)	
Has the clinical purpose for which they were collected been met before removal of any excess?	--
✖ Data already collected for administrative purposes	
✖ Student records (You will need to satisfy FERPA requirements: see SOP 3101, section 3.1 for guidance)	
✖ UNC Dental Records	
✖ Data coming directly from a health plan, health care clearinghouse, or health care provider?	
✖ Publicly available data	
✖ Other	
✔ None of the above	
For EACH data source checked above, provide a description of the data, proposed use, how data were collected (including consent procedures), and where data currently reside.	
--	

C.1.2. Describe your plans for obtaining permission from the custodians of the data, records or specimens (e.g., pathology dept, tissue bank, original researcher):

We are not analyzing existing records, data, or human biological specimens.

C.1.3. Do the custodians of the data, records or specimens require a data use agreement?

No

C.2. Coding and Data Use Agreements

C.2.1. When you receive these data, records or human biological specimens will they be coded? Coded means identifying information that would enable the research team to readily ascertain the individual's identity has been replaced with a number, letter, symbol, or combination thereof (i.e., a code). If you will not be using existing materials, check "No."

No

Part D. The Consent Process

D.1. Obtaining informed consent from subjects

The standard consent process is for all subjects to sign a document containing all the elements of informed consent, as specified in the federal regulations. Some or all of the elements of consent, including signatures, may be altered or waived under certain circumstances. If you will be requesting a waiver answer "not applicable" for any of the following questions that will not pertain to this study. You will be asked to provide relevant information in the section below on waivers.

D.1.1. Will children under the age of majority in their locale (18 years in NC) be enrolled? (Note: Any minor subject who attains the age of majority during the course of the research study must provide consent as an adult, unless consent has been waived, which is requested in section D.3.1.)

No

D.1.2. Will adult subjects be enrolled in your study?

Yes

Explain the process for obtaining consent from the subject.

Before being selected as subjects, all volunteers will be required to read and sign a form asserting that they have read and understood the following: 1.) Subject participation is strictly voluntary; 2.) The purpose of the study; 3.) The nature and extent of subject participation; 4.) The subject=s rights to withdraw at any time; 5.) The subject=s right to privacy, 6.) The risks associated with participation; 7.) The method and schedule of compensation; and 8.) The limits of the University and PI=s liability.

The PI will briefly describe the study and answer any questions that each subject might have regarding his/her participation, the safety of the procedures, issues related to payment, etc. The PI will then review the contents of the consent form before he or she and the subject sign it. Subjects will have the opportunity to ask questions at any time during the study by contacting the PI and or the medical staff.

D.1.3. Will decisionally-impaired subjects be enrolled in your study? (includes unconscious patients, some psychiatric disorders, others who lack the capacity to give consent)

No

D.1.4. Are you planning to obtain consent from any Non-English speaking subjects?

No

D.1.5. Describe who (by role) will be obtaining consent or parental permission.

The principal investigator (Andrew Ghio) obtains consent.

D.1.6. Discuss the potential for influencing the subject's decision to participate. Describe steps that will be taken to minimize undue influence during the consent process. These might include a waiting period between the initial consent discussion and obtaining consent, or obtaining consent by someone other than a person with perceived authority (e.g., professor, employer, treating physician).

There are two weeks waiting period between consenting the volunteer and actually allowing any involvement in the study.

D.1.7. Has the sponsor of this study provided a model consent form?

No

D.2. Waiver of written documentation of informed consent

The default is for subjects to sign a written document that contains all the elements of informed consent. Under limited circumstances, the requirement for a signed consent form may be waived by the IRB. For example, this might occur for phone or internet surveys, when a signed consent form is either impractical or unnecessary, or in circumstances where a signed consent form creates a risk for the subject.

D.2.1. Are you requesting a waiver of any aspect of written (signed) documentation?

Yes

Choose which of the following consent approaches apply and attach the relevant document: *

- ✗ Full consent form minus the signature lines

You will be provided with a system built consent form when you reach the Consent Form section. This can be edited to remove the signature lines.

- ✓ Information or fact sheet (streamlined unsigned consent form)
- ✗ Online consent form with electronic agreement
- ✗ Consent statement incorporated into a survey itself
- ✗ Verbal consent obtained in person or via the phone
- ✗ Short form (for subjects with limited ability to read full consent form)

Choose which one of the following justifies the waiver of written documentation: *

- ✗ The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality (e.g., study topic is sensitive so that public knowledge of participation could be damaging). Participants should be asked whether they want documentation linking them with the research and the participants' wishes will govern whether they sign the form. Note: This justification cannot be used in FDA-regulated research.
- ✓ The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. (e.g., many phone or mail surveys, "man in the street" interviews, etc.).
- ✗ The subjects or LARs are members of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk of harm to subjects, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

If your request for a waiver of written documentation applies to some but not all of your subject groups and/or consent forms, please describe and justify

Waiver is requested for use with the telephone screening tool, as that tool will be used to collect identifiers along with a medical history.

D.3. Full or partial waiver of consent

The default is for subjects to give informed consent. A waiver might be requested for research involving only existing data or human biological specimens. More rarely, it might be requested when the research design requires withholding some study details at the outset (e.g., behavioral research involving deception). In limited circumstances, parental permission may be waived. This section should also be completed for a waiver of HIPAA authorization if research involves Protected Health Information (PHI) subject to HIPAA regulation, such as patient records.

D.3.1. Are you requesting any of the following:

- ✗ a waiver of informed consent in its entirety
- ✗ a waiver or alteration of some of the elements of informed consent
- ✗ a waiver of HIPAA authorization (If you are accessing patient records for this research, you must also request a waiver of HIPAA authorization)

D.3.2. If your request for a waiver applies to some but not all of your subject groups and/or consent forms, please describe and justify

No Answer Provided

D.3.3. Does this request for waiver support a study design that involves deception or withholding of information?

No

Consent Forms

This submission requires the following consent forms

Template Type
Adult Consent Form **I am not using this template because:** Waiver of written consent requested in application (Section D.2.)
Information or Fact Sheet
SSN Collection for payments
SSN Collection for use as identifier
Stored Specimens without Identifiers **I am not using this template because:** Not Yet Available / Not Applicable

This submission includes the following consent forms

File Name	Document Type
bronch pe consent 10 17 2019.doc	Consent Form Other
cru consent 11 19 2019.doc	Consent Form Other

view consent forms

Attachments

This submission requires the following attachments

Document Type
Pencil and Paper Questionnaire Survey
Telephone Questionnaire Survey
IDS Approval
Investigator Brochure and/or Drug Package Insert **This attachment not provided because:** Not Yet Available / Not Applicable
Recruitment Ad for Participant Pool
Newspaper Ad for Recruitment
Website for Recruitment **This attachment not provided because:** Not Yet Available / Not Applicable
Telephone Script for Recruitment
Email or Listserv Recruitment
Recruitment Follow Up

This submission includes the following attachments

File Name	Document Type
Ad for CRU-A 2019.pdf	Recruitment Ad for Participant Pool

WebSite CRU and CRU-A 2019.pdf	Email or Listserv Recruitment
CRU Bronch PE Reminder October 2012.pdf.pdf	Recruitment Follow Up
Ad for CRU 2019_1.pdf	Newspaper Ad for Recruitment
CRU BRONCH Asthma sub STUDY VISIT APPOINTMENT REMINDER.docx	Other Materials for Recruitment
CRU BRONCHOSCOPY STUDY VISIT APPOINTMENT REMINDER.docx	Other Materials for Recruitment
CRU Bronchoscopy bronch physical reminder.docx	Other Materials for Recruitment
CRU CraigsList 2019.pdf	Other Materials for Recruitment
CRU BRONCHOSCOPY RECRUITMENT SCRIPT 2019.pdf	Telephone Script for Recruitment
CRU Reminder Healthy October 2012.pdf.pdf	Pencil and Paper Questionnaire Survey
CRU BRONCH QUESTIONNAIRE1.rtf	Telephone Questionnaire Survey
CRU BRONCH EMAIL ANNOUNCEMENT 2019.pdf	IDS Approval
CRU bronchoscopy payment voucher 2019.pdf	Other
atropine sulfate insert.pdf	Other

view attachments

Addenda

Data Security Requirements

view addenda

If Principal Investigator of this study is a Student or Trainee Investigator, the Faculty Advisor certifies the following:

I accept ultimate responsibility for ensuring that this study complies with all the obligations listed above for the PI.

By certifying below, the Principal Investigator affirms the following:

I will personally conduct or supervise this research study. I will ensure that this study is performed in compliance with all applicable laws, regulations and University policies regarding human subjects research. I will obtain IRB approval before making any changes or additions to the project. I will notify the IRB of any other changes in the information provided in this application. I will provide progress reports to the IRB at least annually, or as requested. I will report promptly to the IRB all unanticipated problems or serious adverse events involving risk to human subjects. I will follow the IRB approved consent process for all subjects. I will ensure that all collaborators, students and employees assisting in this research study are informed about these obligations. All information given in this form is accurate and complete.

This study proposes research that has been determined to include Security Level 2 data security requirements. I agree to accept responsibility for managing these risks appropriately in consultation with departmental and/or campus security personnel. The Data Security Requirements addendum can be reviewed here.

Certifying Signatures:

Signature: Electronic Signature Received **Date:** 10/18/2019 09:24:34 AM

Andrew J. Ghio

U.S. ENVIRONMENTAL PROTECTION AGENCY
CENTER FOR PUBLIC HEALTH & ENVIRONMENTAL ASSESSMENT
PUBLIC HEALTH & INTEGRATED TOXICOLOGY DIVISION
CLINICAL RESEARCH BRANCH

CONSENT FOR PRE-BRONCHOSCOPY SCREENING STUDIES

You are being considered as a subject for a bronchoscopy study which involves placing a flexible instrument into your airways to examine and obtain samples from the lungs. Because of the nature of this procedure, it is important that you not have any pre-existing problems which could cause unnecessary risk.

For that reason, you consent at this time only to screening procedures to determine if you are qualified to undergo bronchoscopy. You understand that you will have to agree to the actual bronchoscopy by signing another consent form.

In signing this consent form, you agree to the following procedures:

1. Have your blood pressure checked.
2. Have a pulmonary (breathing) history taken.
3. Undergo a limited physical examination, which may include examination of your head, neck, throat, chest, and heart.
4. Have not more than 45 mL (3 tablespoons) blood drawn from a vein. The venipuncture may cause some discomfort but will not affect your health.
5. Perform a set of pulmonary function measurements.

You understand that the results of the above screening tests will be discussed with you and will determine whether you can continue with the bronchoscopy study. The EPA person you can contact if you have questions about the screening process or outcome is:

Andrew Ghio, MD
Research Medical Officer, USEPA
(919) 966-0670

If you feel your rights have been infringed, you may contact the Committee on the Protection of the Rights of Human Subjects at (919) 966-3113.

You are participating in this pre-bronchoscopy screening of your own free will and know that you may withdraw at any time without question. Whether or not you qualify for bronchoscopy, you will be paid $20.00.

You understand that in the event of physical injury directly resulting from research procedures, financial compensation cannot be provided under the Federal Compensation Act. In the event, however, that physical injury is caused by the negligence of a Federal employee, the Federal Government would be liable in accord with the Federal Tort Claims Act. Every effort will be

made to make available to you the facilities and professional skills of the University of North Carolina Medical Center at Chapel Hill.

Signature of Volunteer _____

Investigator's Statement:
I, the undersigned, have fully defined and explained all pre-bronchoscopy screening procedures to the volunteer.

Signature of Witness _____

University of North Carolina-Chapel Hill
Consent to Participate in a Research Study
Adult Subjects

Medical IRB Study # 91-0679
Consent Form Version Date: November 19, 2019

Title of Study: Effects of *in vitro* pollutant exposure on functional and biochemical characteristics of human pulmonary cells in normal subjects

Principal Investigator: *Andrew J. Ghio, MD*
UNC-CH Department: Medicine
Phone number: 919-966-0670

Co-Investigators: Tracey Montilla, Julie Wood, and Martha Almond

Sponsor: EPA
You are being asked to take part in a research study. The investigators listed above are in charge of the study; other professional persons may help them or act for them.

This study focuses on the acquisition of cells from the lungs of healthy volunteers for test tube investigation on the biological effects of environmental agents.

Research studies are designed to gain scientific knowledge that may help other people in the future. You may or may not receive any direct benefit from participating. There may also be risks associated with participating in research studies.

Your participation is voluntary. You may refuse to participate, or may withdraw your consent to participate in any study at any time and for any reason.

Details about this particular study are discussed below. It is important that you understand this information so that you can decide in a free and informed manner whether you want to participate. You will be given a copy of this consent form. You are urged to ask the investigators named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?
The purpose of this research study is the acquisition of cells from both blood and lungs for further test tube studies of environmental agents.

How many subjects will participate in this study?
We plan to include up to 150 participants per year. This particular study has been an ongoing study since 1991 and recruitment continues.

How long will your participation last?
Your participation in this study will last for approximately 3 hours for a screening history and exam and one morning for the bronchoscopy.

What will happen if you take part in the study?

During the course of this study, the following will occur: Before being approved for bronchoscopy, you must undergo some screening tests that involve a physical examination, breathing tests, and blood tests. Approval requires that you have no significant problems with your nose, throat, heart, lungs or blood. The results of screening tests must be within normal limits or acceptable to the physician involved. The screening process takes one and one-half hours. The bronchoscopy takes thirty minutes to set up, and thirty minutes to complete. There is a minimum of 90 minutes' observation afterward. The total time commitment for the physical and the procedures associated with the bronchoscopy (a total of two visits) is about half a day.

It is essential that you (1) not take medications including over-the-counter preparations (you can take birth control pills) for one week prior to bronchoscopy, (2) not have cold or flu symptoms for six weeks before the procedure, (3) avoid dusty or smoky places for 48 hours prior to the bronchoscopy, (4) take nothing by mouth after midnight the night before bronchoscopy, (5) take nothing by mouth for two hours after the procedure, and (6) stay for a suitable observation period after the procedure at the discretion of the physician involved and not ride a bicycle or motorcycle home. You must stay in the local Raleigh/Durham/Chapel Hill area for 24 hours after the procedure.

A single blood sample totaling no more than 100 ml (7 oz) may be obtained from you and a small tube (IV) will be placed in a vein for potential use in administering fluids.

Immediately before the bronchoscopy, you may or may not be given an intravenous (I.V.) injection of atropine in your arm to control your heart rate from slowing with placement of the bronchoscope in your airway; the provision of this medication depends on your heart rate. This medication can cause some increase in heart rate and a dry mouth. During the procedure you will receive cardiac monitoring. Supplemental oxygen may be provided. You will be closely monitored and if blood oxygen approaches low value, prompt corrective action will be initiated.

After the airways are visualized, the tip of the bronchoscope is wedged in a bronchus on the left side for bronchial lavage ("washing areas of the lung"). A total volume of 270 cc of sterile saline, one aliquot of 20 cc and 5 additional aliquots of 50 cc each, will be injected and immediately aspirated through the channel in the bronchoscope using a syringe. The lavage fluid aliquots will be put in polypropylene tubes and kept on ice until processed. This is repeated on the right side. You may also undergo a brushing of the large and small airways through the bronchoscope (brush biopsy). The purpose of the brushing is to recover some of the epithelial cells which line your airways. The brushing procedure will take up to 10 minutes. Bleeding should be slight but, if persistent, will be controlled with epinephrine.

Are there any reasons you should not participate?

You should not participate in this study if…

1. You are not 18 to 40 years of age.
2. Your weight is not greater than 110 pounds.
2. You are taking medications which the nurses and doctors feel might exclude you from this study.
3. You have an abnormal physical examination.
4. You have abnormal laboratory studies.
5. You have allergies to medications used in the study.
6. You have a naris too tight to comfortably pass fiberoptic bronchoscope.
7. You have high risk behavior for bloodborne pathogens.
8. You have had an upper respiratory infection within the past six weeks.

What are the possible risks or discomforts?

This study might involve the following risks and/or discomforts to you:

There are several risks associated with performing bronchoscopy, although these risks are exceedingly small when bronchoscopy is performed on young healthy subjects, the type of people involved in this study.

The primary risk of bronchoscopy is discomfort in the nose and throat, which is caused by having the bronchoscope inserted through the nose and passed through the back of your throat to reach the trachea (windpipe) and the airways leading to the lungs. This discomfort is alleviated with topical lidocaine, which you will gargle and inhale prior to beginning the procedure. If you are suffering from discomfort in your nose and throat because they are not adequately anesthetized, you can request that more lidocaine be used, however, there is a limit to the maximum amount of lidocaine that can be given. If you are unable to tolerate the passage of the bronchoscope thorough your nose and throat because of pain in spite of having received the maximum allowable amount of lidocaine, the procedure will be immediately terminated.

A second risk of having bronchoscopy performed is coughing. Coughing is caused by irritation from the bronchoscope itself or the instruments used to obtain the biopsy material. Lidocaine liquid can be sprayed into your airways thorough the bronchoscope to relieve coughing. If the coughing is uncontrollable even with the use of the maximum amount of lidocaine, the procedure will be stopped immediately.

Lower airway bleeding can also occur from injury to the airway wall caused by the bronchoscope or the biopsy procedures. This bleeding is usually very minor (only a few milliliters of blood are lost). The bleeding resolves spontaneously within several minutes. If the bleeding is mild to moderate, epinephrine (adrenalin) can be sprayed on the bleeding site through the bronchoscope to hasten the clotting.

The lidocaine used for anesthesia during the procedure can have some adverse effects because some of the lidocaine can be absorbed into the blood stream from the nose and lungs. If you are allergic to lidocaine, you could develop itching, hives, difficulty breathing, and possibly shock (a dangerous drop in blood pressure). This risk is minimal, but you will be excluded from participating in this study if you are allergic to lidocaine or any other topical anesthetic that is commonly used in minor surgical or dental procedures. Lidocaine can also cause symptoms in your central nervous system (confusion, tremor, euphoria, or, rarely, seizures) or heart rate disturbances (very fast or very slow heart rate) if an excessive dose of medication is used. Finally, a death in a volunteer receiving an overdose (over 1000 milligrams) of lidocaine during bronchoscopy has been reported from Rochester, New York. However, no serious side effects of this medication have been noted at lower doses such as those described in this protocol which uses up to 360 milligrams of lidocaine during the entire procedure. If any problems develop secondary to the use of lidocaine, Dr. Ghio and the physician on duty that day at the Human Studies Division of the EPA will be available to handle these problems.

Atropine, the medication possibly given to you by vein before the procedure starts, is given to help prevent your pulse from falling when the bronchoscope is first put into your airway. Atropine can cause you to have a dry mouth and nose as well as an increased pulse for about 30 to 60 minutes after it is given. These side effects are not harmful to you, and they wear off within 30 to 60 minutes after the drug is given.

The placement of an IV catheter in your arm can cause some pain. However, the IV is placed by a registered nurse who is experienced in this technique, and the pain is minor, usually resolving soon after the IV catheter is in place. Rarely, placement of an IV catheter can result in the formation of a hematoma (bruise) at the site of the IV after it is removed. Also, a rare complication of IV placement is skin infection or an infection of the vein in which the IV catheter has been placed. The risk of getting an infection from the IV are minimized by the nurse's use of sterile technique of place the catheter. If you do

have signs of infection at the IV site (redness, warmth, painful skin, swelling) after completion of the procedure, you will need to contact the EPA medical station ((919) 966-6232) or the physician who performed the bronchoscopy. You are not at increased risk by having blood drawn through the IV catheter.

Some subjects who undergo bronchoscopy may have a low-grade fever (less than 101 degrees Fahrenheit) after the procedure is completed. This fever is almost always benign and usually resolves within 24 hours. Nevertheless, a persistent fever or any temperature of greater than 101 degrees Fahrenheit might mean that you have an infection, particularly pneumonia. Therefore, if you have any fever greater than 101 degrees Fahrenheit after the bronchoscopy or a fever that doesn't resolve in 24 hours after the procedure is completed, you should contact the EPA medical station or the physician who performed the bronchoscopy so that arrangements can be made for you to be examined by one of the physicians at EPA. To prevent fever, you are provided ibuprofen (or acetaminophen if preferred) as you leave. You will be called 24 hours after the procedure to check on your condition. In addition, there may be uncommon or previously unrecognized risks that might occur.

What are the possible benefits?

The benefits to you of participating in this study may be

1. You will receive a free medical history and physical examination; all of the results will be available upon your request.
2. You will receive pulmonary function testing at no charge. The results of these tests will be made available to you upon request. You will be permitted to discuss any abnormal findings with a physician.
3. You will learn more about the effect of air pollution on your own health, which might influence where you might live and work in the future.
4. The donation of fluid and cells will not have any immediate benefits to you, but that studies on the cells may lead to a better understanding of the function of certain lung cells.

What if we learn about new risks during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will your privacy be protected?

No subjects will be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-CH will take all steps allowable by law to protect the privacy of personal information.

The lung washing and brush biopsy samples will be identified by code, and the source will not be identified by name. Every effort will be taken to protect the identity of participants in this study. However, there is no guarantee that the information cannot be obtained by legal process or court order. No subjects will be identified in any report or publication of this study or its results.

Will you be paid for participating?

Subjects who arrive in the medical station having not follow instructions (for example, having eaten food after midnight, taking medications, or failing to report cold of flu symptoms) will receive $15.00 for their time. In addition, standby subjects who are asked to report to the site but who do not undergo the procedure will be paid $40.00. Subjects continuing in the study will be compensated for participation in addition to being reimbursed for reasonable travel expenses from outside Chapel Hill and for parking

costs at the campus (hotel costs are not included). The estimated total compensation averages $425. Procedures are paid as follows:

Bronchoscopy including 1 venipuncture	$400.00
Brush biopsies (up to six brushings)	$25.00

Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons, UNC will report the amount to the Internal Revenue Service on Form 1099. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

Will it cost you anything to participate?
All costs of the research will be paid by the US Environmental Protection Agency.

Who is sponsoring this study?
This research is funded by the United States Environmental Protection Agency. This means that the research team is being compensated by the sponsor for conducting the study. The researchers do not, however, hold a direct financial interest in the sponsor or in the product being studied.

What will happen if you are injured by this research?
All forms of medical research, diagnosis, and treatment involve some risk of injury or illness. Despite our high level of precaution, you may develop an injury or illness due to participating in this study. If you develop an injury or illness determined by the on duty physician to be due to your participation in this research, the EPA will reimburse your medical expenses to treat the injury or illness up to $5000. If you believe your injury or illness was due to a lack of reasonable care or other negligent action, you have the right to pursue legal remedy. The Federal Tort Claims Act, 28 U.S.C. 2671 et. seq. provides for money damages against the United Sates when personal injury or property loss results from the negligent or wrongful act or omission of any employee of the EPA while acting within the scope of his or her employment. Signing this consent form does not waive any of your legal rights or release the investigator, the sponsor, the institution, or its agents from liability for negligence. If a research related injury or illness occurs, you should contact the Director of the EPA NHEERL Human Research Protocol Office at 919.966.6217.

What if you want to stop before your part in the study is complete?
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have further questions, or if a research-related injury occurs, you should call Dr. Andrew J. Ghio at (919) 966-0670.

What if you have questions about your rights as a subject?
This research has been reviewed and approved by the Committee on the Protection of the Rights of Human Subjects (Medical IRB) at the University of North Carolina at Chapel Hill. If you have any

questions or concerns regarding your rights as a research subject, you may contact the Chairman of the Committee at (919) 966-1344.

- -

Subject's Agreement:
I have read the information provided above. I voluntarily agree to participate in this study.

_____ _____
Signature of Research Subject Date

_____
Printed Name of Research Subject

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent